REMARKS

Responsive to the action dated July 2, 2002, applicants elect the invention of Group I, drawn to a method of identifying a zinc finger domain that recognizes a target site. Applicants traverse the restriction between Groups I, II, III, and IV below. In addition, applicants reserve the right to traverse the restriction among Groups 5 through 54 at a later date.

With respect to the restriction between Groups I and II, Applicants point out that steps (a), (c), (d), and (e) of claim 1 (Group I) correspond to steps (a), (d), (e), and (f) of claim 16 (Group II). Claim 16 differs from claim 1 in that steps of amplifying (b) and joining (c) are required in claim 16. However, note that claim 11, which depends from claim 1 and is within Group I, also recites use of amplification to provide a plurality of hybrid nucleic acids. Accordingly, examination of both Group II along with Group I should not represent an undue burden on the Examiner.

Restriction is appropriate when inventions are "independent and distinct." Applicants concur that the inventions of Groups I, III, and IV are distinct, and accordingly non-obvious, with respect to one another. However, the inventions are connected in design, and, therefore, are not entirely independent. Newly entered claim 95 is drawn to one of the common design elements. This claim begins with cells comprising both the reporter construct and the hybrid nucleic acid encoding the test zinc finger domain: i.e., the plurality cells produced in step (c) of claim 1 (Group I), in step (d) of claim 21 (Group I), step (c) of claim 24 (Group III), and step (c) of claim 26 (Group IV). Claims 1, 21, 24 and 26 could reasonably be written to depend from claim 95. Since new claim 95 is generic to and links all three of Groups I, III, and IV, it is logical to examine claim 95 and claims dependent therefrom along with the claims of Groups I, III, and IV, without posing an undue burden.

Support for the amendments to claim 1, 16, and 21 can be found, for example, at page 6, line 23, to page 7, line 11, and page 26, lines 30 to 31. New claim 86 is supported by claim 1 as originally filed. Support for new claim 87 can be found, e.g., at page 6, line 23, to page 7, line 11. Support for new claims 88 to 90 can be found, e.g., at page 25, lines 27 to 28. Support for new claims 91 and 92 can be found, e.g., at page 5, line 24.

New claims 95-97 are supported, e.g., by originally filed claims 1 and 26. New claim 98 is supported, e.g., by originally filed claim 24.

Support for new claims 99, 100, 107, 108, and 119 can be found, for example, at page 6, lines 17 to 22, and page 9, lines 25 to 26. Support for new claims 101 to 103 and 109 to 111 can be found, e.g., at page 25, lines 27 to 28 and page 14, line 26. Support for new claims 104 to 106 can be found, e.g., at page 26, lines 30 to 31. Support for new claims 112-116 can be found, e.g., at page 9, lines 5 to 7. Support for new claim 117 can be found, e.g., in originally filed claim 33. Support for new claim 118 can be found, e.g., page 8, line 24 and page 9, lines 21 to 24.

Enclosed is a Petition for Extension of Time and a check for the required fee. Please apply any additional charges or credits to Deposit Account No. 06-1050, referencing attorney docket no. 12279-002001.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 36-85 have been cancelled.

Claims 1, 16, 21, 24, and 26 have been amended as follows:

1. (Amended) A method of identifying a zinc finger domain that recognizes a target site on a DNA, the method comprising:

(a) providing cells containing a reporter construct, the construct comprising a reporter gene operably linked to a promoter, wherein the reporter gene is expressed above or below a given level when a transcription factor recognizes both a recruitment site and a target site of the promoter, but not when the transcription factor recognizes only the recruitment site of the promoter;

(b) providing a plurality of hybrid nucleic acids, each of which encodes a non-naturally occurring protein comprising (i) a [transcription activation] transcriptional regulatory domain, (ii) a DNA binding domain that recognizes the recruitment site, and (iii) a test zinc finger domain, wherein the encoded amino acid sequence of the test zinc finger domain varies among the members of the plurality;

(c) contacting the plurality of hybrid nucleic acids with the cells under conditions that permit at least one of the plurality of nucleic acids to enter at least one of the cells;

(d) maintaining the cells under conditions permitting expression of the hybrid nucleic acids in the cells; and

(e) identifying a cell that contains a hybrid nucleic acid of (b) and that expresses the reporter gene above or below the given level as an indication that the cell contains a hybrid nucleic acid encoding a test zinc finger domain that recognizes the target site.

16. (Amended) A method of identifying a zinc finger domain that recognizes a target site on a DNA, the method comprising:

(a) providing cells containing a reporter construct, the construct comprising a reporter gene operably linked to a promoter, wherein the reporter gene is expressed above or below a given level when a transcription factor recognizes both a recruitment site and a target site of the promoter, but not when the transcription factor recognizes only the recruitment site of the promoter;

(b) amplifying a plurality of nucleic acid sequences, each of which encodes a test zinc finger domain, using an oligonucleotide primer that anneals to a nucleic acid encoding a conserved domain boundary;

(c) joining each nucleic acid sequence of (b) to nucleic acid sequences encoding (i) a [transcription activation] transcriptional regulatory domain, and (ii) a DNA binding domain that recognizes the recruitment site, to form a plurality of hybrid nucleic acids;

(d) contacting the plurality of hybrid nucleic acids of (c) with the cells of (a) under conditions that permit at least one of the plurality of hybrid nucleic acids to enter at least one of the cells;

(e) maintaining the cells under conditions permitting expression of the hybrid nucleic acids in the cells; and

(f) identifying a cell that contains a hybrid nucleic acid of (c) and that expresses the reporter gene above or below the given level, wherein the hybrid nucleic acid encodes a zinc finger domain that recognizes the target site on a DNA.

21. (Amended) A method of determining whether a test zinc finger domain recognizes a target site on a promoter, the method comprising:

(a) providing a reporter construct comprising a reporter gene operably linked to a promoter, wherein the reporter gene is expressed above or below a given level when a transcription factor recognizes both a recruitment site and a target site of the promoter, but not when the transcription factor recognizes only the recruitment site of the promoter;

(b) providing a hybrid nucleic acid that encodes a non-naturally occurring protein comprising (i) a [transcription activation] transcriptional regulatory domain, (ii) a DNA binding domain that recognizes the recruitment site, and (iii) a test zinc finger domain;

(c) contacting the reporter construct with a cell under conditions that permit the reporter construct to enter the cell;

(d) prior to, after, or concurrent with step (c), contacting the hybrid nucleic acid with the cell under conditions that permit the hybrid nucleic acid to enter the cell;

(e) maintaining the cell under conditions permitting expression of the hybrid nucleic acid in the cell; and

(f) detecting reporter gene expression in the cell, wherein a level of reporter gene expression greater or less than the given level is an indication that the test zinc finger domain recognizes the target site.

24. (Amended) A method of determining whether a test zinc finger domain recognizes a target site on a promoter, the method comprising:

(a) providing a first cell comprising a reporter construct comprising a reporter gene operably linked to a promoter, wherein the reporter gene is expressed above or below a given level when a transcription factor recognizes both a recruitment site and a target site of the promoter, but not when the transcription factor recognizes only the recruitment site of the promoter;

(b) providing a second cell comprising a hybrid nucleic acid that encodes a protein comprising (i) a [transcription activation] transcriptional regulatory domain, (ii) a DNA binding domain that recognizes the recruitment binding site, and (iii) a test zinc finger domain;

(c) fusing the first and second cells to form a fused cell;

(d) maintaining the fused cell under conditions permitting expression of the hybrid nucleic acids in the cell; and

(e) detecting reporter gene expression in the fused cell, wherein a level of reporter gene expression greater or less than the given level is an indication that the test zinc finger domain recognizes the target site.

26. (Amended) A method of determining whether a test zinc finger domain recognizes a target site on a promoter, the method comprising:

(a) providing a plurality of reporter constructs, each construct comprising a reporter gene operably linked to a promoter, wherein the reporter gene is expressed above or below a given level when a transcription factor recognizes both a recruitment site and a target site of the promoter, but not when the transcription factor recognizes only the recruitment site of the promoter;

(b) providing a cell containing a hybrid nucleic acid, that encodes a non-naturally occurring protein comprising (i) a [transcription activation] transcriptional regulatory domain, (ii) a DNA binding domain that recognizes the recruitment site, and (iii) a test zinc finger domain;

(c) contacting the plurality of reporter constructs with the cell under conditions that permit at least one of the plurality of reporter constructs to enter the cell;

(d) maintaining the cell under conditions permitting expression of the hybrid nucleic acid in the cell; and

(e) identifying a cell that contains a reporter gene of (a) and that expresses the reporter gene above or below the given level as an indication that the reporter construct in the cell comprises a target site recognized by the test zinc finger domain.